

**AMENDMENTS TO THE CLAIMS**

**This listing of claims will replace all prior versions and listings of claims in the application:**

**LISTING OF CLAIMS:**

1. **(original):** A set of genetic polymorphisms being associated with optic neuropathy, which comprises at least one polymorphism selected from the group consisting of:
  - (1) AAG to AAT substitution at codon 198 of the Endothelin-1 gene (Lys198Asn);
  - (2) -1370T>G polymorphism of the Endothelin-1 gene promoter region;
  - (3) A138 insertion/deletion(A138I/D) polymorphism in exon 1 of the Endothelin-1 gene;
  - (4) +70C>G polymorphism in 3' non-coding region of the Endothelin receptor A gene;
  - (5) +1222C>T polymorphism of the Endothelin Receptor A gene;
  - (6) CAC to CAT substitution at codon 323 in exon 6 of the Endothelin Receptor A gene (His323His);
  - (7) -231A>G polymorphism of the Endothelin Receptor A gene promoter region;
  - (8) CTG to CTA substitution at codon 277 in exon 4 of the Endothelin receptor B gene;
  - (9) 9099C>A polymorphism of the Mitochondrial gene;
  - (10) 9101T>G polymorphism of the Mitochondrial gene;
  - (11) 9101T>C polymorphism of the Mitochondrial gene;
  - (12) 9804G>A polymorphism of the Mitochondrial gene;
  - (13) 11778G>A polymorphism of the Mitochondrial gene;
  - (14) -713T>G polymorphism of the Angiotensin II type 1 receptor gene promoter region;
  - (16) 3123C>A polymorphism of the Angiotensin II type 2 receptor gene;

- (25) CAA to CGA substitution at codon 192 of the Paraoxonase 1 gene (Gln192Arg);
- (26) TTG to ATG substitution at codon 55 of the Paraoxonase 1 gene (Leu55Met);
- (27) CGG to CAG substitution at codon 144 of the Noelin 2 gene (Arg144Gln);
- (32) GGA to CGA substitution at codon 389 of the  $\beta$ 1 adrenergic receptor gene (Gly389Arg);
- (35) 1105T>C polymorphism of the Myocilin gene (Phe369Leu);
- (36) 412G>A polymorphism of the Optineurin gene;
- (37) 1402C>T polymorphism of the E-Selectin gene;
- (38) The combination of polymorphisms of -857C>T of the Tumor necrosis factor  $\alpha$  gene promoter region and 412G>A of the Optineurin gene;
- (39) The combination of polymorphisms of -863C>A of the Tumor necrosis factor  $\alpha$  gene promoter region and 603T>A of the Optineurin gene;
- (40) CGC to CCC substitution at codon 72 of the TP53 gene (Arg72Pro);
- (41) TAC to CAC substitution at codon 113 of the Microsomal epoxide hydrolase 1 gene (Tyr113His);
- (42) -110A>C polymorphism of the Heatshock protein 70-1 gene promoter region;
- (43) -338C>A polymorphism of the Endothelin converting enzyme gene promoter region;
- (44) -670A>G polymorphism of the CD95 gene promoter region;
- (45) AAG to AAA substitution at codon 119 of the Microsomal epoxide hydrolase 1 gene (Lys119Lys);
- (47) GGA to AGA substitution at codon 16 of the  $\beta$ 2 adrenergic receptor gene (Gly16Arg); and

(48) CAA to GAA substitution at codon 27 of the  $\beta$ 2 adrenergic receptor gene  
(Gln27Glu).

2. **(currently amended):** A method for diagnosing or predicting susceptibility to optic neuropathy in a human subject, ~~which~~ comprising the steps of:

- i) obtaining a biological sample from the subject,
- ii) determining the genotype of the sample ~~in~~ with respect ~~of~~ to ~~the~~ a set of the polymorphisms comprising:
  - (27) CGG to CAG substitution at codon 144 of the Noelin 2 gene (Arg144Gln);
  - (35) 1105T>C polymorphism of the Myocilin gene (Phe369Leu); and
  - (36) 412G>A polymorphism of the Optineurin gene ~~of claim 1,~~ and
- iii) diagnosing or predicting susceptibility to optic neuropathy in the subject based on the genotype.

3. **(original):** The method of Claim 2, wherein the optic neuropathy is glaucoma or Leber's disease.

4. **(original):** The method of Claim 2, wherein the set of polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with optic neuropathy.

5. **(currently amended):** A method for diagnosing or predicting susceptibility to glaucoma in a human subject, ~~which~~ comprising the steps of:

i) obtaining a biological sample from the subject,  
ii) determining the genotype of the sample ~~in~~ with respect ~~of~~ to a set of polymorphisms comprising at least ~~one~~ polymorphism selected from the group consisting of:

- (1) ~~AAG to AAT substitution at codon 198 of the Endothelin-1 gene (Lys198Asn);~~
- (2) ~~1370T>G polymorphism of the Endothelin-1 gene promoter region;~~
- (3) ~~A138 insertion/deletion(A138I/D) polymorphism in exon 1 of the Endothelin-1 gene;~~
- (4) ~~+70C>G polymorphism in 3' non-coding region of the Endothelin receptor A gene;~~
- (5) ~~+1222C>T polymorphism of the Endothelin Receptor A gene;~~
- (6) ~~CAC to CAT substitution at codon 323 in exon 6 of the Endothelin Receptor A gene (His323His);~~
- (7) ~~231A>G polymorphism of the Endothelin Receptor A gene promoter region;~~
- (8) ~~CTG to CTA substitution at codon 277 in exon 4 of the Endothelin receptor B gene;~~
- (9) ~~9099C>A polymorphism of the Mitochondrial gene;~~
- (10) ~~9101T>G polymorphism of the Mitochondrial gene;~~
- (11) ~~9101T>C polymorphism of the Mitochondrial gene;~~
- (12) ~~9804G>A polymorphism of the Mitochondrial gene;~~
- (13) ~~11778G>A polymorphism of the Mitochondrial gene;~~
- (14) ~~713T>G polymorphism of the Angiotensin II type 1 receptor gene promoter region;~~
- (16) ~~3123C>A polymorphism of the Angiotensin II type 2 receptor gene;~~
- (25) ~~CAA to CGA substitution at codon 192 of the Paraoxonase 1 gene (Gln192Arg);~~

- ~~(26) TTG to ATG substitution at codon 55 of the Paraoxonase 1 gene (Leu55Met);~~
- (27) CGG to CAG substitution at codon 144 of the Noelin 2 gene (Arg144Gln);
- ~~(32) GGA to CGA substitution at codon 389 of the  $\beta$ 1-adrenergic receptor gene~~  
(Gly389Arg);
- (35) 1105T>C polymorphism of the Myocilin gene (Phe369Leu); and
- (36) 412G>A polymorphism of the Optineurin gene[[:]]
- ~~(37) 1402C>T polymorphism of the E-Selectin gene;~~
- ~~(38) The combination of polymorphisms of 857C>T of the Tumor necrosis factor  $\alpha$  gene~~  
promoter region and 412G>A of the Optineurin gene;
- ~~(39) The combination of polymorphisms of 863C>A of the Tumor necrosis factor  $\alpha$  gene~~  
promoter region and 603T>A of the Optineurin gene;
- ~~(42) 110A>C polymorphism of the Heatshock protein 70-1 gene promoter region;~~
- ~~(43) 338C>A polymorphism of the Endothelin converting enzyme gene promoter region;~~
- ~~(44) 670A>G polymorphism of the CD95 gene promoter region;~~
- ~~(45) AAG to AAA substitution at codon 119 of the Microsomal epoxide hydrase 1~~  
gene(Lys119Lys);
- ~~(47) GGA to AGA substitution at codon 16 of the  $\beta$ 2-adrenergic receptor gene~~  
(Gly16Arg); and
- ~~(48) CAA to GAA substitution at codon 27 of the  $\beta$ 2-adrenergic receptor gene~~  
(Gln27Glu), and
- iii) diagnosing or predicting susceptibility to glaucoma in the subject based on the genotype.

6. **(original):** The method of Claim 5, wherein the set of polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with glaucoma.

7. **(currently amended):** The method of ~~Claim 5~~Claim 38, wherein the at least one genetic polymorphism is selected from the group consisting of:

- (1) AAG to AAT substitution at codon 198 of the Endothelin-1 gene (Lys198Asn);
  - (2) -1370T>G polymorphism of the Endothelin-1 gene promoter region;
  - (5) +1222C>T polymorphism of the Endothelin Receptor A gene;
  - (6) CAC to CAT substitution at codon 323 in exon 6 of the Endothelin Receptor A gene (His323His);
  - (7) -231A>G polymorphism of the Endothelin Receptor A gene promoter region;
  - (16) 3123C>A polymorphism of the Angiotensin II type 2 receptor gene;
  - (26) TTG to ATG substitution at codon 55 of the Paraoxonase 1 gene (Leu55Met);
  - (32) GGA to CGA substitution at codon 389 of the  $\beta$ 1 adrenergic receptor gene (Gly389Arg);
  - (43) -338C>A polymorphism of the Endothelin converting enzyme gene promoter region;
  - (45) AAG to AAA substitution at codon 119 of the Microsomal epoxide hydrolase 1 gene(Lys119Lys), and
- wherein the glaucoma is normal tension glaucoma.

8. **(original):** The method of Claim 7, wherein the set of polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with normal tension glaucoma.

9. **(currently amended):** The method of ~~Claim 5~~Claim 38, wherein the at least one genetic polymorphism is selected from the group consisting of:

- (4) +70C>G polymorphism in 3' non-coding region of the Endothelin receptor A gene;
- (14) -713T>G polymorphism of the Angiotensin II type 1 receptor gene promoter region;
- (25) CAA to CGA substitution at codon 192 of the Paraoxonase 1 gene (Gln192Arg);
- ~~(35) 1105T>C polymorphism of the Myocilin gene (Phe369Leu);~~
- ~~(36) 412G>A polymorphism of the Optineurin gene;~~
- (38) The combination of polymorphisms of -857C>T of the Tumor necrosis factor  $\alpha$  gene promoter region and 412G>A of the Optineurin gene;
- (42) -110A>C polymorphism of the Heatshock protein 70-1 gene promoter region;
- (44) -670A>G polymorphism of the CD95 gene promoter region;
- (47) GGA to AGA substitution at codon 16 of the  $\beta$ 2 adrenergic receptor gene (Gly16Arg); and
- (48) CAA to GAA substitution at codon 27 of the  $\beta$ 2 adrenergic receptor gene (Gln27Glu), and

wherein the glaucoma is primary open angle glaucoma.

10. **(original):** The method of Claim 9, wherein the set of polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with primary open angle glaucoma.

11. **(original):** A method for diagnosing or predicting susceptibility to Leber's disease in a human subject, which comprising the steps of:

- i) obtaining a biological sample from the subject,
- ii) determining genotype of the sample in respect of the set of the polymorphisms comprising at least one polymorphism selected from the group consisting of:
  - (40) CGC to CCC substitution at codon 72 of the TP53 gene (Arg72Pro); and
  - (41) TAC to CAC substitution at codon 113 of the Microsomal epoxide hydrolase 1 gene (Tyr113His), and
- iii) diagnosing or predicting susceptibility to Leber's disease in the subject based on the genotype.

12. **(original):** The method of Claim 11, wherein the set of polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with Leber's disease.

13. **(currently amended):** The method of Claim 2, wherein the genotype is determined by ~~the~~ a method selected from the group consisting of polymerase chain reaction (PCR), restriction fragment length polymorphism (PCR-RFLP) analysis, polymerase chain



reaction followed by single strand conformation polymorphism (PCR-SSCP) analysis, ASO hybridization analysis, direct sequencing ~~analysis~~analysis, ARMS analysis, DGGE analysis, RNaseA cleaving analysis, chemical restriction analysis, DPL analysis, TaqMan® PCR analysis, Invader® assay, MALDI-TOF/MS analysis, TDI analysis, single nucleotide extension assay, WAVE assay and one molecular fluorescent detection assay, and a mixture thereof.

**14. (original):** A kit for diagnosing or predicting susceptibility to optic neuropathy in a human subject which comprises primer set and/or probe suitable for determining genotype in respect of a set of genetic polymorphisms comprising at least one genetic polymorphism selected from the group consisting of:

- (1) AAG to AAT substitution at codon 198 of the Endothelin-1 gene (Lys198Asn);
- (2) -1370T>G polymorphism of the Endothelin-1 gene promoter region;
- (3) A138 insertion/deletion(A138I/D) polymorphism in exon 1 of the Endothelin-1 gene;
- (4) +70C>G polymorphism in 3' non-coding region of the Endothelin receptor A gene;
- (5) +1222C>T polymorphism of the Endothelin Receptor A gene;
- (6) CAC to CAT substitution at codon 323 in exon 6 of the Endothelin Receptor A gene (His323His);
- (7) -231A>G polymorphism of the Endothelin Receptor A gene promoter region;
- (8) CTG to CTA substitution at codon 277 in exon 4 of the Endothelin receptor B gene;
- (9) 9099C>A polymorphism of the Mitochondrial gene;
- (10) 9101T>G polymorphism of the Mitochondrial gene;
- (11) 9101T>C polymorphism of the Mitochondrial gene;

- (12) 9804G>A polymorphism of the Mitochondrial gene;
- (13) 11778G>A polymorphism of the Mitochondrial gene;
- (14) -713T>G polymorphism of the Angiotensin II type 1 receptor gene promoter region;
- (16) 3123C>A polymorphism of the Angiotensin II type 2 receptor gene;
- (25) CAA to CGA substitution at codon 192 of the Paraoxonase 1 gene (Gln192Arg);
- (26) TTG to ATG substitution at codon 55 of the Paraoxonase 1 gene (Leu55Met);
- (27) CGG to CAG substitution at codon 144 of the Noelin 2 gene (Arg144Gln);
- (32) GGA to CGA substitution at codon 389 of the  $\beta$ 1 adrenergic receptor gene  
(Gly389Arg);
- (35) 1105T>C polymorphism of the Myocilin gene (Phe369Leu);
- (36) 412G>A polymorphism of the Optineurin gene;
- (37) 1402C>T polymorphism of the E-Selectin gene;
- (38) The combination of polymorphisms of -857C>T of the Tumor necrosis factor  $\alpha$  gene  
promoter region and 412G>A of the Optineurin gene;
- (39) The combination of polymorphisms of -863C>A of the Tumor necrosis factor  $\alpha$  gene  
promoter region and 603T>A of the Optineurin gene
- (40) CGC to CCC substitution at codon 72 of the TP53 gene (Arg72Pro);
- (41) TAC to CAC substitution at codon 113 of the Microsomal epoxide hydrolase 1 gene  
(Tyr113His);
- (42) -110A>C polymorphism of the Heatshock protein 70-1 gene promoter region;
- (43) -338C>A polymorphism of the Endothelin converting enzyme gene promoter region;
- (44) -670A>G polymorphism of the CD95 gene promoter region;

(45) AAG to AAA substitution at codon 119 of the Microsomal epoxide hydase 1 gene(Lys119Lys);

(47) GGA to AGA substitution at codon 16 of the  $\beta$ 2 adrenergic receptor gene (Gly16Arg); and

(48) CAA to GAA substitution at codon 27 of the  $\beta$ 2 adrenergic receptor gene (Gln27Glu).

**15. (original):** The kit of Claim 14, wherein the optic neuropathy is glaucoma or Leber's disease.

**16. (original):** The kit of Claim 14, wherein the set of the genetic polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with optic neuropathy.

**17. (original):** A kit for diagnosing or predicting susceptibility to glaucoma in a human subject which comprises primer set and/or probe suitable for determining genotype in respect of a set of genetic polymorphisms comprising at least one genetic polymorphism selected from the group consisting of:

- (1) AAG to AAT substitution at codon 198 of the Endothelin-1 gene (Lys198Asn);
- (2) -1370T>G polymorphism of the Endothelin-1 gene promoter region;
- (3) A138 insertion/deletion(A138I/D) polymorphism in exon 1 of the Endothelin-1 gene;
- (4) +70C>G polymorphism in 3' non-coding region of the Endothelin receptor A gene;

- (5) +1222C>T polymorphism of the Endothelin Receptor A gene;
- (6) CAC to CAT substitution at codon 323 in exon 6 of the Endothelin Receptor A gene  
(His323His);
- (7) -231A>G polymorphism of the Endothelin Receptor A gene promoter region;
- (8) CTG to CTA substitution at codon 277 in exon 4 of the Endothelin receptor B gene;
- (9) 9099C>A polymorphism of the Mitochondrial gene;
- (10) 9101T>G polymorphism of the Mitochondrial gene;
- (11) 9101T>C polymorphism of the Mitochondrial gene;
- (12) 9804G>A polymorphism of the Mitochondrial gene;
- (13) 11778G>A polymorphism of the Mitochondrial gene;
- (14) -713T>G polymorphism of the Angiotensin II type 1 receptor gene promoter region;
- (16) 3123C>A polymorphism of the Angiotensin II type 2 receptor gene;
- (25) CAA to CGA substitution at codon 192 of the Paraoxonase 1 gene (Gln192Arg);
- (26) TTG to ATG substitution at codon 55 of the Paraoxonase 1 gene (Leu55Met);
- (27) CGG to CAG substitution at codon 144 of the Noelin 2 gene (Arg144Gln);
- (32) GGA to CGA substitution at codon 389 of the  $\beta$ 1 adrenergic receptor gene  
(Gly389Arg);
- (35) 1105T>C polymorphism of the Myocilin gene (Phe369Leu);
- (36) 412G>A polymorphism of the Optineurin gene;
- (37) 1402C>T polymorphism of the E-Selectin gene;
- (38) The combination of polymorphisms of -857C>T of the Tumor necrosis factor  $\alpha$  gene  
promoter region and 412G>A of the Optineurin gene;

(39) The combination of polymorphisms of -863C>A of the Tumor necrosis factor  $\alpha$  gene promoter region and 603T>A of the Optineurin gene;

(42) -110A>C polymorphism of the Heatshock protein 70-1 gene promoter region;

(43) -338C>A polymorphism of the Endothelin converting enzyme gene promoter region;

(44) -670A>G polymorphism of the CD95 gene promoter region;

(45) AAG to AAA substitution at codon 119 of the Microsomal epoxide hydrazase 1 gene(Lys119Lys);

(47) GGA to AGA substitution at codon 16 of the  $\beta$ 2 adrenergic receptor gene (Gly16Arg); and

(48) CAA to GAA substitution at codon 27 of the  $\beta$ 2 adrenergic receptor gene (Gln27Glu).

**18. (original):** The kit of Claim 17, wherein the set of the genetic polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with optic neuropathy.

**19. (original):** A kit for diagnosing or predicting susceptibility to normal tension glaucoma in a human subject which comprises primer set and/or probe suitable for determining genotype in respect of a set of genetic polymorphisms comprising at least one genetic polymorphism selected from the group consisting of:

(1) AAG to AAT substitution at codon 198 of the Endothelin-1 gene (Lys198Asn);

(2) -1370T>G polymorphism of the Endothelin-1 gene promoter region;

- (5) +1222C>T polymorphism of the Endothelin Receptor A gene;
- (6) CAC to CAT substitution at codon 323 in exon 6 of the Endothelin Receptor A gene (His323His);
- (7) -231A>G polymorphism of the Endothelin Receptor A gene promoter region;
- (16) 3123C>A polymorphism of the Angiotensin II type 2 receptor gene;
- (26) TTG to ATG substitution at codon 55 of the Paraoxonase 1 gene (Leu55Met);
- (32) GGA to CGA substitution at codon 389 of the  $\beta$ 1 adrenergic receptor gene (Gly389Arg);
- (43) -338C>A polymorphism of the Endothelin converting enzyme gene promoter region;
- (45) AAG to AAA substitution at codon 119 of the Microsomal epoxide hydrase 1 gene(Lys119Lys).

**20. (original):** The kit of Claim 19, wherein the set of the genetic polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with normal tension glaucoma.

**21. (original):** A kit for diagnosing or predicting susceptibility to primary open angle glaucoma in a human subject which comprises primer set and/or probe suitable for determining genotype in respect of a set of genetic polymorphisms comprising at least one genetic polymorphism selected from the group consisting of:

- (4) +70C>G polymorphism in 3' non-coding region of the Endothelin receptor A gene;
- (14) -713T>G polymorphism of the Angiotensin II type 1 receptor gene promoter region;

- (25) CAA to CGA substitution at codon 192 of the Paraoxonase 1 gene (Gln192Arg);
- (35) 1105T>C polymorphism of the Myocilin gene (Phe369Leu);
- (36) 412G>A polymorphism of the Optineurin gene;
- (38) The combination of polymorphisms of -857C>T of the Tumor necrosis factor  $\alpha$  gene promoter region and 412G>A of the Optineurin gene;
- (42) -110A>C polymorphism of the Heatshock protein 70-1 gene promoter region;
- (44) -670A>G polymorphism of the CD95 gene promoter region;
- (47) GGA to AGA substitution at codon 16 of the  $\beta$ 2 adrenergic receptor gene (Gly16Arg); and
- (48) CAA to GAA substitution at codon 27 of the  $\beta$ 2 adrenergic receptor gene (Gln27Glu).

**22. (original):** The kit of claim 21, wherein the set of the genetic polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with primary open angle glaucoma.

**23. (original):** A kit for diagnosing or predicting susceptibility to Leber's disease in a human subject which comprises primer set and/or probe suitable for determining genotype in respect of a set of genetic polymorphisms comprising at least one genetic polymorphism selected from the group consisting of:

- (40) CGC to CCC substitution at codon 72 of the TP53 gene (Arg72Pro);

(41) TAC to CAC substitution at codon 113 of the Microsomal epoxide hydrolase gene (Tyr113His).

**24. (original):** The kit of Claim 23, wherein the set of the genetic polymorphisms further comprises at least one genetic polymorphism which has been known to be associated with Leber's disease.

**25. (currently amended):** An isolated polynucleotide consisting of a segment of the sequence:

8881 ~~tetaagatta-aaaatgccet-agcccattc-ttaccacaag-geaacacctac-aceccattate~~

8941 ~~cccatactag-ttattataga-aaccateage-ctacteatte-aaccaatage-cctggeepta~~

9001 ~~egcetaaceg-ctaacattac-tgcaggecac-ctacteatge-acctaattgg-aagegecaee~~

9061 ~~ctagcaatat-caaccattaa-ccttccctct-acacttatec-tcttcacaat-tetaatteta~~

9121 ~~ctgactatcc-tagaaatege-tgtegeetta-atccaagect-aegtttteac-aettetagta~~

9181 ~~ageetatacc-tgcacgacaa-cacataatga-cccaccaate-acatgcectat-catatagtaa~~ SEQ ID NO:1,

wherein the segment comprises at least 90 contiguous nucleotides, and the at least 90 contiguous nucleotides includes position 9099 of the sequence, and wherein position 9099 of the sequence is A, or an isolated polynucleotide which is entirely complementary to the above segment.

**26. (original):** An isolated polynucleotide consisting of a segment of the sequence as shown in Claim 25, wherein the segment comprises at least 90 contiguous nucleotide, and the at



least 90 contiguous nucleotide includes position 9101 of the sequence, and wherein position 9101 of the sequence is G, or an isolated polynucleotide which is entirely complementary to the above segment.

**27. (currently amended):** An isolated polynucleotide consisting of a segment of the sequence:

~~301 actggaage acgggtgtg tgggtactc ggggagcctc tatttcagg ggcgtgagtc~~  
~~361 cagaaetgtc ataagatatg agetgaatac cgagacagtg aaggetgaga aggaaatecc~~  
~~421 tggagetggc taccacggac agttccgta ttctggggt ggtacacgg acattgaatt~~  
~~481 ggcgtgtgat gaagcaggee tetgggtcat ttacagcacc gatgaggeca aaggtgceat~~  
~~541 tgctctctcc aaactgaacc cagagaattc ggaactcgaa caaacctggg agacaaacat~~ SEQ ID NO:2,

wherein the segment comprises at least 90 contiguous nucleotides, and the at least 90 contiguous nucleotides includes codon 369, which is corresponding to the underlined nucleotides of the sequence, and wherein codon 369 is substituted such that it codes for Leu, or an isolated polynucleotide which is entirely complementary to the above segment.

**28. (currently amended):** An isolated polynucleotide consisting of a segment of the sequence:

~~79741 ttagtctcta caatggagtc atgtctggga agaattctagg gtccaatatg agccacatgt~~  
~~79801 caagggecag gtgtgcatca aagacaaagg gtgaagttat ggtcagagg ttggagtcatt~~  
~~79861 gtctgggtca aaggecaggg gtacagcttg gccatggttc catcttgatg cacaggagct~~  
~~79921 gaaggacagg atgaeggaae ttttgeccct gagctcggtc ctggagcagt acaaggecaga~~

~~79981 caccgggacc attgtacget tgcgggagga ggtgaggaa ctctecggea gtctggegge~~  
~~80041 cattcaggag gagatgggtg cctacgggta tgaggacctg cagcaacggg tgatggceet~~  
~~80101 ggaggeeeeg ctecaageet gegeccagaa getgggtatg cettggeeet tgacctgae~~  
~~80161 ceetgatete tgaatgccac aaccaactec agtataacet gtttgtgeet agaagetgga~~  
~~80221 cacagttttg acctetaaet ttaaaecte aaccttgac etteetaet aaggetaac~~SEQ ID NO:3,

wherein the segment comprises at least 90 contiguous nucleotides, and the at least 90 contiguous nucleotides includes codon 144, which is corresponding to the underlined nucleotides of the sequence, and wherein codon 144 is substituted such that it codes for Gln, or an isolated polynucleotide which is entirely complementary to the above segment.

**29. (original):** A method for treating glaucoma in a patient who has an abnormality in the Myocilin gene, which comprises suppressing the expression of the abnormal Myocilin genes in the patient.

**30. (original):** The method of Claim 29, wherein the suppression is carried out by means of RNA interference method.

**31. (original):** A method for predicting the response of a subject to the treatment with a drug, which comprises the steps of; determining genotype in respect of at least one genetic polymorphism being associated with optic neuropathy, and predicting the response of the patient based on the genotype.

**32. (original):** The method of Claim 31, wherein the optic neuropathy is glaucoma or Leber's disease.

**33. (original):** The method of Claim 31, wherein the optic neuropathy is glaucoma.

**34. (original):** The method of Claim 31, wherein the at least one genetic polymorphism is 3123C>A polymorphism of the Angiotensin II type 2 receptor gene.

**35. (original):** The method of Claim 31, wherein the drug is an Angiotensin Receptor II antagonist.

**36. (new):** The method according to Claim 2, wherein the set of polymorphisms further comprises at least one genetic polymorphism selected from the group consisting of:

- (1) AAG to AAT substitution at codon 198 of the Endothelin-1 gene (Lys198Asn);
- (2) -1370T>G polymorphism of the Endothelin-1 gene promoter region;
- (3) A138 insertion/deletion(A138I/D) polymorphism in exon 1 of the Endothelin-1 gene;
- (4) +70C>G polymorphism in 3' non-coding region of the Endothelin receptor A gene;
- (5) +1222C>T polymorphism of the Endothelin Receptor A gene;
- (6) CAC to CAT substitution at codon 323 in exon 6 of the Endothelin Receptor A gene (His323His);
- (7) -231A>G polymorphism of the Endothelin Receptor A gene promoter region;
- (8) CTG to CTA substitution at codon 277 in exon 4 of the Endothelin receptor B gene;

- (9) 9099C>A polymorphism of the Mitochondrial gene;
- (10) 9101T>G polymorphism of the Mitochondrial gene;
- (11) 9101T>C polymorphism of the Mitochondrial gene;
- (12) 9804G>A polymorphism of the Mitochondrial gene;
- (13) 11778G>A polymorphism of the Mitochondrial gene;
- (14) -713T>G polymorphism of the Angiotensin II type 1 receptor gene promoter region;
- (16) 3123C>A polymorphism of the Angiotensin II type 2 receptor gene;
- (25) CAA to CGA substitution at codon 192 of the Paraoxonase 1 gene (Gln192Arg);
- (26) TTG to ATG substitution at codon 55 of the Paraoxonase 1 gene (Leu55Met);
- (32) GGA to CGA substitution at codon 389 of the  $\beta$ 1 adrenergic receptor gene  
(Gly389Arg);
- (37) 1402C>T polymorphism of the E-Selectin gene;
- (38) The combination of polymorphisms of -857C>T of the Tumor necrosis factor  $\alpha$  gene  
promoter region and 412G>A of the Optineurin gene;
- (39) The combination of polymorphisms of -863C>A of the Tumor necrosis factor  $\alpha$  gene  
promoter region and 603T>A of the Optineurin gene;
- (40) CGC to CCC substitution at codon 72 of the TP53 gene (Arg72Pro);
- (41) TAC to CAC substitution at codon 113 of the Microsomal epoxide hydrolase 1 gene  
(Tyr113His);
- (42) -110A>C polymorphism of the Heatshock protein 70-1 gene promoter region;
- (43) -338C>A polymorphism of the Endothelin converting enzyme gene promoter region;
- (44) -670A>G polymorphism of the CD95 gene promoter region;

(45) AAG to AAA substitution at codon 119 of the Microsomal epoxide hydrazase 1 gene(Lys119Lys);

(47) GGA to AGA substitution at codon 16 of the  $\beta$ 2 adrenergic receptor gene (Gly16Arg); and

(48) CAA to GAA substitution at codon 27 of the  $\beta$ 2 adrenergic receptor gene (Gln27Glu).

**37. (new):** The method according to Claim 2, wherein the set of polymorphisms further comprises genetic polymorphisms selected from the group consisting of:

the combination of polymorphisms of -857C>T of the Tumor necrosis factor  $\alpha$  gene promoter region and 412G>A of the Optineurin gene; and

the combination of polymorphisms of -863C>A of the Tumor necrosis factor  $\alpha$  gene promoter region and 603T>A of the Optineurin gene.

**38. (new):** The method according to Claim 5, wherein the set of polymorphisms further comprises at least one genetic polymorphism selected from the group consisting of:

- (1) AAG to AAT substitution at codon 198 of the Endothelin-1 gene (Lys198Asn);
- (2) -1370T>G polymorphism of the Endothelin-1 gene promoter region;
- (3) A138 insertion/deletion(A138I/D) polymorphism in exon 1 of the Endothelin-1 gene;
- (4) +70C>G polymorphism in 3' non-coding region of the Endothelin receptor A gene;
- (5) +1222C>T polymorphism of the Endothelin Receptor A gene;

(6) CAC to CAT substitution at codon 323 in exon 6 of the Endothelin Receptor A gene  
(His323His);

(7) -231A>G polymorphism of the Endothelin Receptor A gene promoter region;

(8) CTG to CTA substitution at codon 277 in exon 4 of the Endothelin receptor B gene;

(9) 9099C>A polymorphism of the Mitochondrial gene;

(10) 9101T>G polymorphism of the Mitochondrial gene;

(11) 9101T>C polymorphism of the Mitochondrial gene;

(12) 9804G>A polymorphism of the Mitochondrial gene;

(13) 11778G>A polymorphism of the Mitochondrial gene;

(14) -713T>G polymorphism of the Angiotensin II type 1 receptor gene promoter region;

(16) 3123C>A polymorphism of the Angiotensin II type 2 receptor gene;

(25) CAA to CGA substitution at codon 192 of the Paraoxonase 1 gene (Gln192Arg);

(26) TTG to ATG substitution at codon 55 of the Paraoxonase 1 gene (Leu55Met);

(32) GGA to CGA substitution at codon 389 of the  $\beta$ 1 adrenergic receptor gene  
(Gly389Arg);

(37) 1402C>T polymorphism of the E-Selectin gene;

(38) The combination of polymorphisms of -857C>T of the Tumor necrosis factor  $\alpha$  gene  
promoter region and 412G>A of the Optineurin gene;

(39) The combination of polymorphisms of -863C>A of the Tumor necrosis factor  $\alpha$  gene  
promoter region and 603T>A of the Optineurin gene;

(42) -110A>C polymorphism of the Heatshock protein 70-1 gene promoter region;

(43) -338C>A polymorphism of the Endothelin converting enzyme gene promoter region;

- (44) -670A>G polymorphism of the CD95 gene promoter region;
- (45) AAG to AAA substitution at codon 119 of the Microsomal epoxide hydrolase 1 gene(Lys119Lys);
- (47) GGA to AGA substitution at codon 16 of the  $\beta$ 2 adrenergic receptor gene (Gly16Arg); and
- (48) CAA to GAA substitution at codon 27 of the  $\beta$ 2 adrenergic receptor gene (Gln27Glu).

**39. (new):** The method according to Claim 5, wherein the set of polymorphisms further comprises genetic polymorphisms selected from the group consisting of:

the combination of polymorphisms of -857C>T of the Tumor necrosis factor  $\alpha$  gene promoter region and 412G>A of the Optineurin gene; and

the combination of polymorphisms of -863C>A of the Tumor necrosis factor  $\alpha$  gene promoter region and 603T>A of the Optineurin gene.